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Trends in hospitalizations and mortality for inflammatory bowel disease from a nationwide database study between 2008 and 2018

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ABSTRACT

This study aimed to describe the trends, inpatient outcomes, and disease burden of hospitalizations for ulcerative colitis (UC) and Crohn's disease (CD). Our study included data on hospitalizations with a principal discharge diagnosis of CD and UC gathered from the Nationwide Inpatient Sample for the years 2008, 2010, 2012, 2014, 2016, and 2018. Individuals ≤18 years and elective hospitalizations were excluded. From 2008 to 2018, we noted a rising trend for UC hospitalizations (P trend < 0.001). However, there was no statistically significant trend for CD hospitalizations (P trend $= 0.249$). The overall inpatient mortality for UC downtrended from 1.09% in 2008 to 0.42% in 2014 (P trend < 0.001). Additionally, inpatient mortality for CD also downtrended with a decrease from 0.28% in 2008 to 0.17% in 2016 (P trend $= 0.002$). Odds of inpatient mortality from 2008 to 2018 were significantly higher for UC than for CD. In conclusion, both CD and UC saw a significant decline in mortality over the study period, but UC hospitalizations had a higher odds of inpatient mortality for all study years.

KEYWORDS Crohn's disease; hospitalizations; mortality; Nationwide Inpatient Sample; trends; ulcerative colitis

Inflammatory bowel disease (IBD), which includes ulcerative colitis (UC) and Crohn's disease (CD), has been called an emerging worldwide epidemic.[1] IBD is a chronic immunologically mediated disease that occurs secondary to a complex interplay between the gut microbiome, the environment, and genetic factors.[2] It is thought to be due to changes in environmental factors, which contribute to the pathogenesis of IBD.[1] The lifestyle in developed countries like the United States has been linked with changes in the microbial colonization of the gut, and the gut microbiome plays a major role in inflammation and mucosal lesion development in IBD.[1] It is estimated that over 1 million US residents have IBD, which contributes to substantial health care costs.[3] With the high and growing prevalence of IBD, understanding trends and outcomes is important in revising current treatment guidelines and guiding future clinical management with the goal of improving patient outcomes.

METHODS

This retrospective interrupted longitudinal trend study analyzed hospitalizations principally for CD and UC in the US from 2008 to 2018. Data were sourced from the Nationwide Inpatient Sample (NIS), which was developed by the Healthcare Cost and Utilization Project, a federal-state-industry partnership. The NIS contains data on inpatient stays, derived from billing data, submitted by hospitals to statewide data organizations across the US, covering 97% of the US population.[4] It approximates a 20% stratified sample of these discharges, which is further weighted to obtain national estimates.[5] The NIS is coded using the International Classification of Diseases (ICD) coding system. In the NIS, diagnoses are divided into two separate categories: principal diagnosis (the main ICD code) and secondary diagnoses (any ICD code other than the principal diagnosis). Our study included the 2008, 2010, 2012, 2014, 2016, and 2018 NIS databases, which were searched using the ICD-9

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Table 1. Biodemographic characteristics of Crohn's disease hospitalizations

Variables	2008	2010	2012	2014	2016	2018
Hospitalizations	58,510	57,211	58,455	57,370	60,245	56,540
Mean age (years)	42.1	42.0	42.7	42.4	43.2	44.2
Women	57.4%	57.3%	56.3%	55.3%	53.3%	54.4%
Racial distribution						
White	62.4%	67.6%	71.9%	70.7%	70.7%	72.0%
Black	9.3%	13.0%	14.1%	14.4%	15.2%	14.9%
Hispanic	4.6%	4.7%	4.8%	5.7%	5.7%	6.6%
Others	23.7%	14.7%	9.2%	9.2%	8.4%	6.5%
Charlson Comorbidity Index Score						
0	77.3%	75.3%	74.6%	73.6%	70.5%	68.2%
1	15.8%	17.0%	16.6%	17.1%	18.0%	19.3%
2	4.5%	4.5%	5.1%	5.3%	6.4%	7.0%
≥3	2.4%	3.2%	3.7%	3.9%	5.1%	5.5%
Insurance type						
Medicaid	21.6%	23.2%	24.5%	24.1%	25.0%	26.0%
Medicare	14.6%	17.2%	16.8%	21.0%	21.6%	20.3%
Private	56.2%	50.2%	49.5%	48.1%	48.1%	48.1%
Uninsured	7.6%	9.4%	9.2%	6.8%	5.3%	5.6%

and ICD-10 codes for a principal discharge diagnosis of CD and UC. Patients ≤18 years and elective hospitalizations were excluded.

Stata Version 16 software (StataCorp, College Station, Texas) was used for data analysis. The biodemographic trends for the study period were highlighted. A multivariate regression analysis was used to calculate the trend in mortality, length of stay (LOS), and total hospital costs (THC) following adjustment for age, sex, race, grouped Charlson comorbidity index, insurance type, mean household income, and hospital characteristics. Total hospital cost was obtained using the Healthcare Cost and Utilization Project Cost-to-Charge Ratio files and adjusted for inflation using the Medical Expenditure Panel Survey index for hospital care, with 2018 as the reference point.[6,7] All *P* values were two-sided, with 0.05 set as the threshold for statistical significance. Institutional review board approval was not needed for this database study.

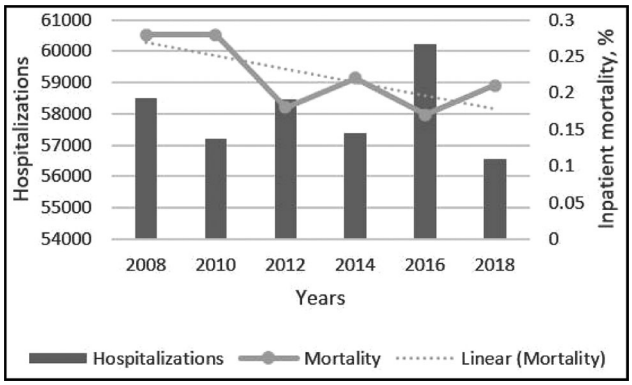

Figure 1. Yearly trends of Crohn's disease hospitalizations (*P* trend = 0.249) and inpatient mortality (*P* trend = 0.002).

RESULTS

Between 2008 and 2018, there was a trend toward decreasing hospitalizations for CD *(Table 1* and *Figure 1)*, *but this was not statistically significant* (*P* trend = 0.249). The mean age over the period ranged from 42.0 to 44.2 years. Most hospitalizations were for women. Over the decade, there was a steady rise in the proportion of Whites and Hispanics with CD. Overall, private insurance was the most prevalent insurer. Inpatient mortality for CD decreased from 0.28% in 2008 to a low of 0.17% in 2016, with an overall significant trend of decreasing mortality (*P* trend = 0.002). There was also a statistically significant decrease in both LOS and THC over the studied period *(Table 2* and *Figure 2)*.

Furthermore, from 2008 to 2018, there was a statistically significant trend toward increasing hospitalizations for UC (*P* trend <0.001) *(Table 3* and *Figure 3)*. The mean age over the period ranged from 47.2 to 49.1 years, which was significantly older than patients with CD. Most of the

Table 2. Outcomes for Crohn's disease hospitalizations

Outcome	2008	2010	2012	2014	2016	2018
Inpatient mortality	0.28%	0.28%	0.18%	0.22%	0.17%	0.21%
Mean length of stay (days)	5.3	5.2	5.0	4.9	4.9	4.8
Mean total hospital cost ($US)	11,590	11,057	10,621	10,457	11,061	11,257

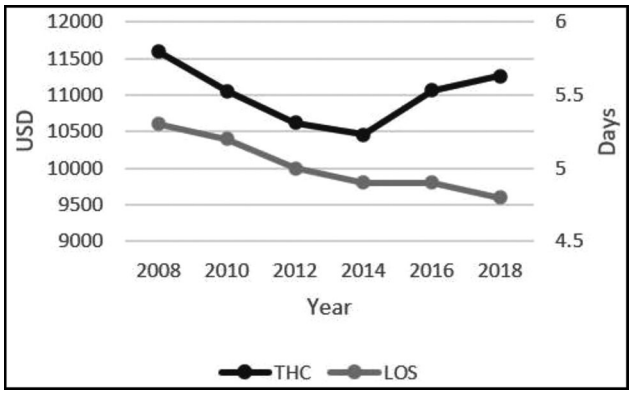

Figure 2. Health care utilization trends for Crohn's disease (*P* trend for length of stay [LOS] < 0.001 and *P* trend for total hospital costs [THC] = 0.002).

hospitalizations were for women. The proportion of UC hospitalizations among Whites and Hispanics also increased during the study period. Overall, private insurance was the most prevalent insurer. Inpatient mortality for UC decreased from 1.09% in 2008 to a low of 0.42% in 2014, with an overall significant trend of decreasing mortality (*P* trend <0.001). There was also a statistically significant decrease in both LOS and THC over the studied period *(Table 4* and *Figure 4)*.

In comparing the two groups, the odds of inpatient mortality was significantly higher in all years for UC compared to CD. Both CD and UC saw a significant decline in mortality over the study period. There was no statistically significant difference in rate of decline in mortality between the two groups *(Figure 5)*.

Table 3. Biodemographic characteristics for ulcerative colitis hospitalizations

Variables	2008	2010	2012	2014	2016	2018
Hospitalizations	34,154	32,823	33,305	34,365	35,735	35,515
Mean age (years)	48.4	47.9	47.9	47.2	48.1	49.1
Women	53.8%	52.0%	52.0%	51.5%	53.0%	54.3%
Racial distribution						
White	61.0%	64.3%	67.7%	68.6%	69.7%	69.5%
Black	8.1%	11.6%	11.4%	10.7%	11.1%	11.1%
Hispanic	7.5%	9.2%	9.9%	10.0%	10.0%	11.3%
Others	23.4%	14.9%	11.0%	10.7%	9.2%	8.1%
Charlson Comorbidity Index Score						
0	70.4%	68.9%	68.5%	69.8%	63.8%	60.3%
1	17.9%	17.9%	18.4%	17.1%	19.2%	20.3%
2	6.4%	6.9%	6.5%	6.2%	8.3%	8.8%
≥3	5.3%	6.3%	6.6%	6.9%	8.7%	10.6%
Insurance type						
Medicaid	27.2%	27.0%	27.9%	26.1%	28.2%	29.6%
Medicare	9.4%	12.8%	12.8%	16.7%	17.9%	17.5%
Private	56.9%	50.6%	50.5%	50.7%	48.5%	46.7%
Uninsured	6.5%	9.6%	8.8%	6.5%	5.4%	6.2%

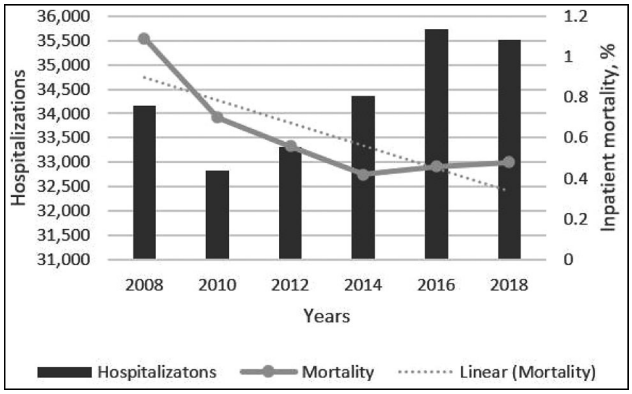

Figure 3. Yearly trends of ulcerative colitis hospitalizations (P trend $<$ 0.001) and inpatient mortality (P trend $<$ 0.001).

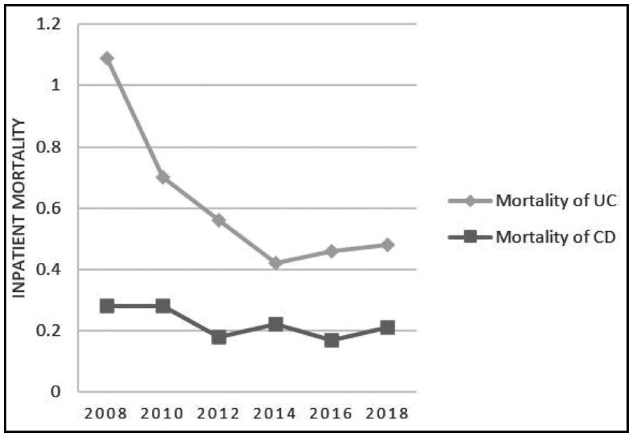

Figure 5. Comparison of inpatient mortality for Crohn's disease (CD) and ulcerative colitis (UC) (P interaction = 0.127).

Table 4. Outcomes for ulcerative colitis hospitalizations

Outcome	2008	2010	2012	2014	2016	2018
Inpatient mortality	1.09%	0.70%	0.56%	0.42%	0.46%	0.48%
Mean length of stay (days)	6.4	5.9	5.6	5.7	5.4	5.1
Mean total hospital cost ($US)	13,914	12,602	12,179	12,156	12,150	12,164

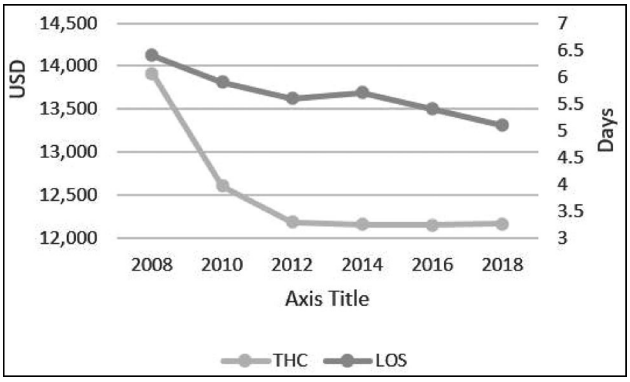

Figure 4. Health care utilization trends for ulcerative colitis (P trend for length of stay [LOS] $<$ 0.001 and P trend for total hospital costs [THC] $<$ 0.001).

DISCUSSION

The incidence of IBD is rising, and 25% of IBD diagnoses occur in those <18 years.[8] Understanding the trends for both UC and CD can help dictate future management and reduce the overall health care and individual burden of IBD.

The mean age over the period ranged from 42.0 to 44.2 years for CD, and from 47.2 to 49.1 years for UC. The age of diagnosis of IBD is reported to be between 18 and 35 typically, so this finding reflects that hospitalizations may occur years after diagnosis.[9] Most hospitalizations for CD were for women, and CD is known to have a greater prevalence in women.[10] It is believed that cumulative estrogen exposure following puberty may play a role in the development of CD, which may in part explain the hospitalization rates for women.[10] Furthermore, it has been well established that women are more likely than men to seek medical care, which may also, in part, explain our findings.

Between 2008 and 2018, inpatient mortality for CD decreased during the study period, with a statistically significant trend of decreasing mortality. Since CD is known to have an age-adjusted mortality that is >50% greater than that of the general population, downward trends in mortality may reflect improvement of care and management in CD patients.[11] There was also a statistically significant decrease in both LOS and THC over the studied period for CD. Inpatient mortality for UC decreased with a statistically significant trend for mortality. There was also a statistically significant decrease in both LOS and THC over the studied period.

The decrease in hospitalizations, THC, LOS, and mortality may reflect overall improvements in care for CD and UC patients. One retrospective study analyzing CD from 1988 to 2008 reported that outcomes in CD may be improved if specialist care is accessed within 1 year of diagnosis.[12] In the last several decades, medical treatment options and approaches for IBD have changed.[13] For example, there has been a recognition of the need for multidisciplinary IBD care, which has led to disease-based outpatient clinics for IBD, which are sometimes referred to as IBD centers.[14] These centers have allowed patients to be treated at a single center, bringing multiple important caregivers to the patient as opposed to the patient having to go to multiple physicians at multiple sites.[14] These centers can provide both medical and surgical care, some of which can be done at the same visit if necessary. Additionally, research has shown that use of IBD centers has resulted in decreased LOS and THC, hospitalization rates, and polypharmacy.[14] All of these factors may play a role in the reductions seen in the studied period.

Additionally, in 2017, there was a change in the language for outcomes related to IBD, as agreed upon as part of the International Consortium for Health Outcomes Measurement; prior to 2017, there was a lack of centralized language related to health care outcome measures for IBD.[15] This change in language may allow for more improvements in quality of care and treatment, which may contribute to the downward trends in THC, LOS, mortality, and hospitalizations. There has been a change in focus from achieving certain clinical responses or remission to more predictive and objective targets, including mucosal healing and corticosteroid-free remission.[15] In 2015, the Selective Therapeutic Targets in Inflammatory Bowel Disease Committee defined the treat-to-target approach for patients with IBD.[16] This shift has been the result of, in part, the availability of stronger biologic agents, which allow for more effective inflammation control.[15]

Despite these downward trends, between 2008 and 2018, there was a statistically significant trend toward increasing hospitalizations for UC, and the odds of inpatient mortality was significantly higher in all years for UC compared to CD. UC has the potential to cause permanent fibrosis and tissue damage and may require surgery for management.[16] At the time of diagnosis, about one-third of patients will have disease extension by 10 years.[16] Additionally, 10% to 15% of patients may ultimately require colectomy.[16] The higher odds of mortality may be due to the increasing hospitalizations trend, as one study reported that those with UC who required medical hospitalization are 5 times more likely to require colectomy.[17] The rise in hospitalizations may reflect the need for surgery that many UC patients have.[17] Some researchers have reported that evolutions in surgery and the shift toward two- or three-stage total proctocolectomy with ileal pouch-anal anastomosis and away from the single-stage total proctocolectomy with Brooke ileostomy may result in increasing hospitalization rates.[17] These changes may account for the trends in hospitalizations in UC and overall greater mortality for UC patients compared to CD patients during the study period.

As with any study, there are limitations that should be noted. Data from the NIS are subject to biases associated with retrospective studies. Moreover, the NIS reports information on hospitalizations rather than individual patients; therefore, patients admitted numerous times would be included more than once in the data set. The NIS also does not include information about the severity of IBD diagnosis at the time of admission. Since the database uses ICD codes to report information, it may have coding errors. Despite these limitations, the outcomes studied, large sample size, and analysis techniques make for a study that provides a current perspective on a major health care burden-causing infection while aiming to encourage further discourse and future controlled prospective studies on IBD hospitalizations in the United States.

In conclusion, from 2008 to 2018, there was an overall increasing trend in hospitalizations for UC but a decreasing trend in hospitalizations for CD. There was a significant decrease in LOS, THC, and mortality in UC and CD over the study period, potentially reflecting changes and improvements in centralized and appropriate management of patients with IBD. Overall, the findings of this study reflect that efforts to improve care in patients with IBD have not been futile. Continued focus on evidence-based interventions may allow for continued improvement in IBD management in the future.

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